curves on July 16 and 19 showed that tolerance was slowly improving, but had not quite returned to normal 8 days after the insulin injections were stopped.

The hyperglycemia following cessation of the insulin injections in these non-diabetics might be explained as due to a compensatory inhibition of the normal islet secretion with a slow readjustment until ordinary activity is attained. Such an interpretation is in accord with the idea of a latent functional capability of the island cells in diabetes mellitus.[1] However, a study of the respiratory quotients in the insulinized non-diabetics now under way indicates that an explanation other than the above may obtain.

6481

On the Motion of Growth. IV. Further Analysis of Energetics of Heat Production with Special Reference to Basal Metabolism During Prolonged Human Fasting.

NORMAN C. WETZEL.

From the Babies and Childrens Hospital, Cleveland, and the Department of Pediatrics, School of Medicine, Western Reserve University.

Certain theoretical considerations in respect to the energetics of heat production as defined[1] for states of changing weight are of special interest but should also prove of rather great practical importance. In view of the fact that the hyperbolic term in equation (6) of the foregoing paper has dampened out and become negligible in the case of human growth beyond the age of twenty, this relation assumes the simpler form,

$$\rho\left(\frac{dq}{dt}\right)^2 + E_c\frac{dq}{dt} + A' = U \qquad (7)$$

for heat production in calories per Kg. per unit of time, the various factors possessing the same significance as before.

It is clear from (7) that U will not alter greatly during any period in which $\left(\frac{dq}{dt}\right)$ fails to change rapidly—a condition, as we have seen, which is actually reached on the average during the second and third decades of life. For constant values of $\pm\left(\frac{dq}{dt}\right)$, U

[1] Gibson, R. B., *J. Lab. Clin. Med.*, 1929, **14**, 597; PROC. SOC. EXP. BIOL. AND MED., 1929, **26**, 449; *Am. J. Physiol.*, 1932, **101**, 41.

[1] Wetzel, N. C., PROC. SOC. EXP. BIOL. AND MED., 1932, **30**, 233.

will also remain constant; but an important question arises as to the conditions under which U, as representative of heat output, will be most economical. So long as $\left(\frac{dq}{dt}\right)$ is positive there cannot be a true minimum, although U may, of course, with low rates of reproduction become as small as ρ, E_c and A' will allow. If, however, no restriction be placed upon the sign of $\left(\frac{dq}{dt}\right)$, a rather significant result may be at once attained by differentiating (7) with respect to t and equating to 0, whence,

$$\frac{dq}{dt} = \frac{-E_c}{2\rho} \tag{8}$$

a condition which leads to the result that U, the unit rate of energy output in the form of heat will actually become and remain a minimum (for constant values of ρ, E_c and A') as long as the unit rate of change in weight $\left(\frac{dq}{dt}\right)$ is negative, and equal to $\left(\frac{-E_c}{2\rho}\right)$.

Attention is thus immediately directed to the possibilities of studying heat production during periods of starvation. But before giving our results, we ought briefly to continue the investigation of these equations. Substituting the value of $\left(\frac{dq}{dt}\right)$ from (8) into (7), we have,

$$A' - \frac{(E_c^2)_s}{4\rho_s} = [U_s]_{\text{minimum}} \tag{9}$$

wherein the subscript s now refers to starvation. The latter result thus indicates that a fasting subject who is losing weight at a unit rate, $\left(\frac{E_c}{2\rho}\right)_s$ must necessarily manifest a rate of heat production which will not only remain constant during this epoch, but which will actually be less than the "equilibrium" level of metabolism represented by A'. It is also of interest to see from the above set of equations that the value of $\left(\frac{dq}{dt}\right)$ from (8) which thus insures a minimum rate of metabolism, is exactly one-half as great as that which would allow a fasting subject likewise to maintain a constant rate of heat production at, however, precisely the "equilibrium" level A', for, if,

$$\frac{dq}{dt} = \left[\frac{-E_c}{\rho}\right]_s \tag{10}$$

we get from (7)

$$A' = U_s \tag{11}$$

The foregoing theoretical results thus afford a rather likely explanation of certain analogous experimental observations long ago described for fasting animals by Rubner[2] and in later years confirmed by Benedict and coworkers[3, 4] in human and in animal (rat) starvation. They cannot be fully discussed here.

As further evidence of the present concept of energy exchange in respect to growth in general and in respect to the particular theoretical results just described, we present next the essential calculations in the human case based upon the excellent experimental data of Benedict.[4] To test (7) it is merely necessary to substitute values of $\left(\frac{dq}{dt}\right)$ which may be computed from data on weight during the period of starvation by any sufficiently exact method, as well as the observed values for U, and calculate the resulting numerical values:

$$\rho_s = 137.256$$
$$(E_c)_s = 641.260$$

when U is given in Cal./Kg./Year, and A' is taken as 9250 in the same units.* Resubstituting and computing "theoretical" values on successive days for U we obtain the final results arranged in Table I and shown graphically in Figure 1. The latter demonstrate conclusively that our assumptions and procedures are quite in accordance with observation.

TABLE I.

Theoretical Values for Basal Metabolism during the Course of a Human Fast Observed by Benedict.

Day of Fast	U_s in Cal./Kg./hr.		
	Computed from Equation (7)	Observed Bed Calorimeter	Observed by Indirect Calorimetry
0	——	1.12	1.05
1	1.163	1.07	1.13
2	1.121	1.09	1.11
3	1.079	1.10	1.10
4	1.046	1.10	1.05
5	1.013	1.02	1.03
6	0.989	1.04	1.01
7	0.974	1.02	1.04
8	0.971	1.06	1.04
9–31	0.970	0.9361 (mean)	0.9678 (mean)

[2] Rubner, Max, *Die Gesetze des Energieverbrauchs bei der Ernährung*, Leipzig, 1902.

[3] Horst, Kathyrn, Mendel, L. B., and Benedict, F. G., *J. Nutrition*, 1930, **3**, 177.

[4] Benedict, F. G., A Study of Prolonged Fasting, Carnegie Institution Publication No. 203, Washington, 1915.

* In this case $\left(\frac{dq}{dt}\right)$ is to be computed in Kg./Kg./Year.

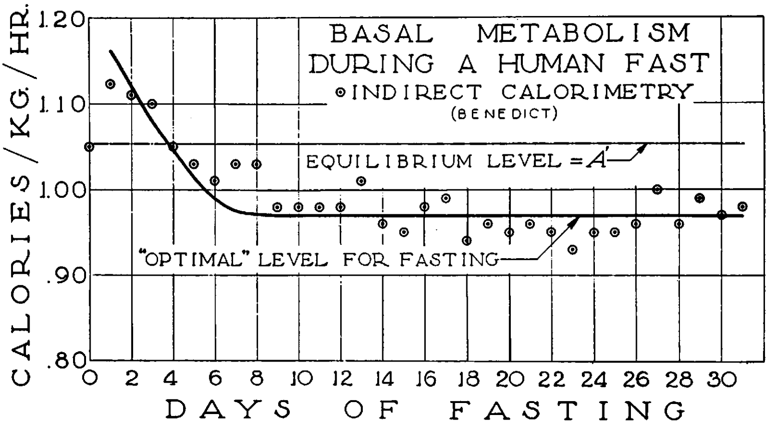

FIG. 1.

The smooth curve traces the theoretical course of heat production in Benedict's study of Levanzin as this has been computed from equation (7). Note that the curve descends below the equilibrium value A' and remains at its lowest level throughout the remainder of the fast, to fulfill the condition for "optimal" energy transfer.

To sum up we have shown that:

(1) The unit rate of energy evolution in heat, U, will be greater than that at the "equilibrium" level A' for all unit rates of change in weight greater than 0;

(2) For negative unit rates of changes in weight (starvation),

$$U = A' \quad \text{when } \frac{-dq}{dt} = 0, \text{ or, } \frac{(E_c)_s}{\rho_s}$$

$$U \gtrless A' \quad \text{when } \frac{-dq}{dt} \gtrless \frac{(E_c)_s}{\rho_s}$$

$$U \text{ is minimum when } \frac{-dq}{dt} = \frac{(E_c)_s}{2\rho_s}$$

The numerical results herein computed for $(E_c)_s$ and ρ lead finally to the prediction by way of equation (8) that the rate of loss in weight during human starvation which ought to insure a minimum rate of heat production is 2.336 Kg./Kg./Year or 0.0064 Kg./Kg./Day, a result next to be tested and confirmed in the following paper.

Some further implications of the equations thus far brought forward find excellent confirmation in the most recent observations of Benedict, Horst, and Mendel[5] on the basal metabolism of oversized starving rats. Their data for the rat again support in every

[5] Benedict, F. G., Horst, Kathryn, and Mendel, L. B., *J. Nutrition*, 1932, **5**, 581.

important respect the major theoretical features of both weight and metabolism curves of human fasting subjects upon which we have laid special emphasis in this and in the succeeding paper. The experiments show clearly (1) that oversized rats also pass into a period of almost purely logarithmic loss in weight (optimal stage where $\left(\frac{dq}{dt}\right)$ = constant; (2) that basal metabolism in terms of Cal./Kg./Day recedes *below* the equilibrium level and remains *constant* during this phase; and (3) as we must expect from equation (7) a subsequent *increase* in U when $\left(\frac{dq}{dt}\right)$ rises at a later stage of the process, in virtue of the absence of the original source of energy S in equation (1).[6] The latter increase in the velocity of starvation will be discussed more extensively in another paper;[7] but, the rise of basal heat production, U, under such conditions is a direct outcome of the energetics of metabolism set forth in equation (7).

6482

On the Motion of Growth. V. Rate of Loss in Weight for Minimum Metabolism.

NORMAN C. WETZEL.

From the Babies and Childrens Hospital, Cleveland, and the Department of Pediatrics, School of Medicine, Western Reserve University.

From theoretical considerations in conjunction with data on heat production during prolonged fasting it has been shown[1] that the optimal relative rate of starvation at which a human individual would conserve his body reserves to the utmost ought to be closely in the neighborhood of 0.0064 Kg./Kg./Day. It is now proposed to examine this result in the light of several observations on the point.

By far the most accurate of the data at hand are those reported by Benedict,[2] but in Figure 1 we have also included the curves of Succi for several fasts, as well as that for Beauté. The ordinates are in $\log_{10}$ (Weight) = $.4343q$, the abscissae in days. There is,

[6] Wetzel, N. C., PROC. SOC. EXP. BIOL. AND MED., 1932, **30**, 224.

[7] Wetzel, N. C., to be published.

[1] Wetzel, N. C., PROC. SOC. EXP. BIOL. AND MED., 1932, **30**, 354.

[2] Benedict, F. G., A Study of Prolonged Fasting, Carnegie Institution Publication No. 203, Washington, 1915.